CLAIMS

What is claimed is:

1. A method of simultaneously measuring in a living vessel at least two chemical parameters associated with inflamed vulnerable atherosclerotic plaque, the method comprising:

providing a fiber optic catheter having an illumination fiber bundle and a detection fiber bundle capable of, respectively, directing radiation onto or receiving radiation from a site on a vessel wall, said catheter having means for reducing optical interference by blood or other fluid within a vessel when undergoing examination;

providing a source of 400-2500 nm wavelength radiation operatively linked to said illumination fiber bundle;

providing a spectrometer operatively linked to detection fiber bundle;

providing a processor operatively linked to said spectrometer containing algorithms and reference measurements for at least two chemical parameters associated with inflamed vulnerable atherosclerotic plaque, said spectrometer and processor together being capable of receiving and analyzing spectral data collected by said detection fiber bundle and reporting corresponding parameter measurements;

optionally providing a display system capable of receiving and displaying a report from said processor;

measuring a first parameter at a multiplicity of sites on a vessel wall;

measuring at least one other parameter at said multiplicity of sites on a vessel wall;

analyzing a multiplicity of parameter measurements corresponding to said multiplicity of sites whereby a qualitative or quantitative value for each said parameter is reported for a corresponding site or region on a vessel wall.

2. The method of claim 1 wherein said measuring of said first and said at least one other parameter comprises choosing said parameters from the group consisting of pH, oxyhemoglobin, deoxyhemoglobin, cytochrome oxidase aa_3, reduced cytochrome oxidase aa_3, nitrosyl hemoglobin, nitrosyl tyrosine, glucose, lactate, oxidized LDL cholesterol, and oxidized collagen.

3. The method of claim 2 wherein said measuring comprises determining a pH level at said site and measuring at least one other parameter chosen from the group consisting of oxyhemoglobin and deoxyhemoglobin, cytochrome oxidase aa_3, reduced cytochrome oxidase aa_3, nitrosyl hemoglobin, nitrosyl tyrosine, glucose, lactate, oxidized LDL cholesterol and oxidized collagen.

4. The method of claim 2 wherein said measuring comprises assessing the relative amounts of oxyhemoglobin and deoxyhemoglobin and at least one other parameter chosen from the group consisting of pH, cytochrome oxidase aa_3, reduced cytochrome oxidase aa_3, nitrosyl hemoglobin, nitrosyl tyrosine, glucose, lactate, oxidized LDL cholesterol and oxidized collagen.

5. The method of claim 2 wherein said measuring comprises assessing the relative amounts of cytochrome oxidase aa_3 and reduced cytochrome oxidase aa_3 and measuring at least one other parameter chosen from the group consisting of pH, nitrosyl hemoglobin, nitrosyl tyrosine, glucose, lactate, oxidized LDL cholesterol and oxidized collagen.

6. The method of claim 2 wherein said measuring comprises assessing the amount of nitrosyl-hemoglobin or nitrosyl-tyrosine and at least one other parameter chosen from the group consisting of pH, oxyhemoglobin, deoxyhemoglobin, cytochrome oxidase aa_3, reduced cytochrome oxidase aa_3, glucose, lactate, oxidized LDL cholesterol and oxidized collagen.

7. The method of claim 2 wherein said measuring comprises assessing the amount of oxidized collagen and at least one other parameter chosen from the group consisting of pH, oxyhemoglobin, deoxyhemoglobin, cytochrome oxidase aa_3, reduced cytochrome oxidase aa_3, nitrosyl hemoglobin, nitrosyl tyrosine, glucose and lactate and oxidized LDL cholesterol.

8. The method of claim 2 wherein said measuring comprises assessing the amount of glucose and at least one other parameter chosen from the group consisting of pH, oxyhemoglobin, deoxyhemoglobin, cytochrome oxidase aa_3, reduced cytochrome oxidase aa_3, nitrosyl hemoglobin, nitrosyl tyrosine, oxidized LDL cholesterol and oxidized collagen.

9. The method of claim 2 wherein said measuring comprises measuring pH, oxidized collagen and, optionally, at least one other parameter chosen from the group consisting of oxyhemoglobin, deoxyhemoglobin, cytochrome oxidase aa_3, reduced cytochrome oxidase aa_3, nitrosyl hemoglobin, nitrosyl tyrosine, glucose, and lactate, and oxidized LDL cholesterol.

10. The method of claim 1 wherein said step of providing a processor is modified by substituting the following:

providing a processor operatively linked to said spectrometer, said processor containing algorithms and reference measurements for at least two chemical parameters associated with inflamed vulnerable atherosclerotic plaque, and containing algorithms and reference measurements for colorimetric measurement of thrombi colored red, brown, greenish-brown, and white, said spectrometer and processor together being capable of receiving and analyzing spectral data collected by said detection fiber bundle and reporting corresponding parameter and colorimetric measurements.

11. The method of claim 1 wherein said optionally providing a display system capable of receiving and displaying a report from said processor includes providing a monitor capable of displaying a color image of said vessel wall.

12. A method of detecting a vulnerable atherosclerotic plaque on a vessel wall comprising simultaneously measuring in a site on a living vessel wall two or more chemical parameters associated with actively metabolizing cells in inflamed vulnerable

atherosclerotic plaque according to the method of claim 1, wherein said measuring comprises qualitatively or quantitatively measuring at least two parameters chosen from the group consisting of oxyhemoglobin, reduced hemoglobin, oxidized cytochrome oxidase aa_3, nitrosyl hemoglobin, nitrosyl tyrosine, pH, glucose, lactate, oxidized LDL cholesterol, and oxidized collagen.

13. The method of claim 12 further comprising detecting an indicator dye associated with a plaque whereby a plaque cap fissure is revealed.

14. The method of claim 13 wherein said step of detecting an indicator dye comprises detecting a radiocontrast dye associated with a plaque by intraplaque leakage.

15. The method of claim 13 wherein said step of detecting an indicator dye comprises detecting a biocompatible molecule having a distinct NIR absorbance spectrum.

16. The method of claim 15 wherein said step of detecting an indicator dye comprises detecting a hydroxyethyl starch.

17. A method of detecting in a living vessel an atherosclerotic plaque at risk of rupturing or thrombosing, the method comprising:

qualitatatively or quantitatively measuring at least two parameters associated with inflamed vulnerable plaque in accordance with the method of claim 1;

measuring dye sequestered beneath the surface of a site along a vessel wall; and

analyzing said dye measurement together with said parameter measurements to distinguish plaque from relatively stable plaque and normal vessel wall and to determine predictive level of risk for at least one site or group of sites on a wall of said vessel.

18. The method of claim 17 wherein said measuring of dye sequestration is performed with said fiber optic catheter, said dye containing a 400-2,500 nm wavelength radiation absorbing chromophore, and said processor additionally containing algorithms and reference measurements for analysing reflected or scattered radiation from said chromophore.

19. The method of claim 17 wherein said measuring of dye sequestration is performed by angiography, said dye is radiopaque, and said signal processor is also capable of receiving and analyzing said angiographic measurement.

20. A method of detecting a vulnerable atherosclerotic plaque on a vessel wall comprising the method of claim 17 and additionally

monitoring the visible color image of said site; and

analyzing said visual image together with said parameter and dye penetration measurements.

21. A method of distinguishing vulnerable plaque in need of therapeutic intervention from relatively stable plaque or non diseased tissue in a living vessel wall comprising the method of claim 1 wherein said analyzing includes comparing said qualitative or

quantitative values for a site or group of adjacent sites to similarly obtained values for another site or group of sites along the vessel wall, whereby a qualitative or quantitative value for each said parameter is reported for a particular site or region on a vessel wall expressed in terms relative to other sites or groups of sites along the same vessel wall.

22. A method of detecting an inflamed vulnerable atherosclerotic plaque on a vessel wall comprising:

identifying areas having pH <7.2;

identifying areas having an amount of oxidized collagen indicative of a thin or weak plaque cap;

identifying areas having red microthrombi;

identifying areas that have taken up and sequestered an indicator dye beneath the surface of a vessel;

correlating at least two of said identified areas with a site or group of sites on a vessel wall;

calculating a predictive level of risk for each said site or group of sites.

23. A method of treating a patient known to be suffering from atherosclerotic vessel disease and suspected of being at risk of experiencing a plaque rupture and/or an occlusive thrombotic event, the method comprising:

detecting an atherosclerotic plaque at risk of rupturing or thrombosing according to the method of claim 17, said method optionally including monitoring the visible color

image of said site and analyzing said visual image together with said parameter and dye measurements;

determining from said predicted level of risk for at least one site or group of sites on a wall of said vessel at least one vulnerable plaque for targeting treatment;

applying a local treatment to at least one so-determined target plaque, said treatment chosen from the group consisting of balloon angioplasty, laser angioplasty, heated balloon (RF, ultrasound or laser) angioplasty, surgical atherectomy, laser atherectomy, the placement of an appropriate stent, another conventional mechanical or irradiation treatment method, and pharmacological treatment regimens including anti-coagulants, fibrinolytic, thrombolytic, anti-inflammatory, anti-proliferative, immunosuppressant, collagen-inhibiting, endothelial cell growth-promoting, and other conventional pharmacologically appropriate local treatments effective for reducing or eliminating inflamed plaque.

24. A multi-parameter catheter comprising:

distal and proximal ends and a conduit disposed therebetween;

an outer wall;

an inflatable balloon attached to said outer wall and circumferentially disposed about a portion of said distal end;

a window in said outer wall on said catheter distal end, said window being transparent to 400-2,500 nm wavelength radiation;

a illumination lumen extending longitudinally through said catheter to said window;

a detection lumen extending longitudinally through said catheter to said window;

a guidewire lumen extending longitudinally through said catheter to a terminus on said distal end;

a balloon inflation lumen in fluid communication with an aperture in said outer wall inside a region enclosed by said balloon;

an optional fluid transporting lumen extending longitudinally through said catheter to a fluid outlet in said distal end;

a fiber optic illumination bundle containing a multiplicity of illumination fibers capable of transmitting approximately 400 to 2500 nm wavelength radiation, each said fiber having a proximal and distal end;

a fiber optic detection bundle containing a multiplicity of detection fibers similar to those of the illumination bundle and having proximal and distal ends, the distal ends of each said bundle forming a circular array of single fibers adjacent an outer wall of said catheter, the array of illumination fibers being disposed between the array of detection fibers and said outer wall,

means for focusing radiation emitted from or received by said illumination and detection fibers;

a manifold attached to said conduit at said catheter proximal end, said manifold having a guidewire aperture and an illumination connector, detection connector, balloon inflation connector and optional perfusion connector branching out therefrom opposite a conduit attachment point on said manifold.

25. The catheter of claim 24 further comprising a visible imaging fiber optic bundle containing a multiplicity of visible imaging fibers similar to the illumination and detection fibers, the distal ends of which are similarly arrayed, said illumination fiber array being disposed between said imaging fiber array and said detection fiber array, and said manifold also having a visible imaging connector branching out therefrom.

26. The catheter of claim 25 wherein said focusing means comprises a mirror.

27. The catheter of claim 25 wherein said focusing means comprises curved or bent fiber distal ends.

28. A multi-parameter analyzer for diagnosing an atherosclerotic plaque at risk of rupture or thrombosis comprising:

the catheter of claim 26;

a light source operatively linked to said proximal end of each said illumination fiber and capable of emitting radiation of about 400 to 2,500 nm wavelength;

a spectrotometer operatively linked to each said detection fiber proximal end and capable of converting a multiplicity of optical signals arising from a site along a vessel wall to a corresponding digital signal;

a processor operatively linked to said spectrometer and containing suitable algorithms and reference data for storing and analyzing a multiplicity of digital signals and determining a qualitative or quantitative value for at least two parameters associated

with actively metabolizing cells of an inflamed vulnerable atherosclerotic plaque whereby a risk value indicative of the level of risk of rupture or thrombosis is determined;

a display system operatively linked to said processor for displaying said parameter values and/or said risk value; and

an optional microcontroller operationally linked to at least one of said light source, spectrometer and signal processor.

29. The device of claim 28 wherein said at least two parameters are chosen from the group consisting of oxyhemoglobin, deoxyhemoglobin, oxidized cytochrome oxidase aa_3, reduced cytochrome oxidase aa_3, pH, glucose, lactate, nitrosyl hemoglobin, nitrosyl tyrosine, oxidized LDL cholesterol and oxidized collagen.

30. A method of detecting atherosclerotic plaque at risk of rupturing or thrombosing, the method comprising:

providing the device of claim 29

inserting a guidewire into a vessel;

sliding said catheter onto and along said guidewire such that the distal portion of said catheter becomes situated at a desired location in said vessel;

advancing or retracting said catheter such that said window is situated adjacent a point on a vessel wall;

inflating or deflating said balloon such that fluid in said vessel is substantially excluded between said window and said vessel wall;

optionally providing means for detecting infrared radiation emitted from a site on said vessel wall, and prior to irradiating said site with visible or near-infrared wavelength radiation, detecting thermal radiation from said site;

operating said illumination source such that said illumination fibers nondestructively irradiate a multiplicity of radially spaced apart sites with 400-2,500 nm wavelength radiation;

transmitting radiation arising from a multiplicity of sites on said vessel wall by a corresponding multiplicity of detection fibers to said spectrometer;

operating said spectrometer such that 400-2,500 nm wavelength radiation arising from said multiplicity of sites are received and converted to a corresponding multiplicity of digital signals;

operating said signal processor such that said digital signals are received and analyzed;

repositioning said catheter distal end, in cooperation with the operation of said signal processor, to second and subsequent positions along said vessel wall while operating said illumination source;

optionally inputting additional angiography data into said signal processor for analysis;

determining a qualitative or quantitative value for at least two chemical or physical parameters associated with inflamed vulnerable atherosclerotic plaque and correlating said value with a site or group of sites on said vessel wall;

optionally operating said display system to provide a visible image of a site or group of sites on said vessel wall and/or to report said values.

31. An improved method of detecting vulnerable atherosclerotic plaque *in vivo* in which a chemical or biochemical component of a plaque is measured, the improvement comprising measuring at least two analytes associated with activated macrophages, said analytes chosen from the group consisting of pH, oxyhemoglobin, deoxyhemoglobin, nitrosyl hemoglobin, nitrosyl tyrosine, oxidized cytochrome aa_3, reduced cytochrome aa_3, glucose, lactate, oxidized LDL cholesterol and oxidized collagen.

32. The method of claim 31 wherein said improvement further comprises employing visible and near-infrared spectroscopy to measure said analytes.

33. The method of claim 31 wherein said improvement further comprises employing magnetic resonance spectroscopy to measure said analytes.

34. An improved method of differentiating atherosclerotic plaque at risk of rupturing and occluding from plaque not presently at risk in which optical radiation from a site along a vessel wall is analyzed, the improvement comprising identifying a site on said vessel wall by analyzing for indicia of actively metabolizing cells.

35. A method of detecting infection, cancer, wound or autoimmune disease comprising detecting inflammation associated with said infection, cancer, wound or autoimmune disease, said detecting comprising measuring at a site in the body at least two parameters chosen from the group consisting of pH, oxyhemoglobin, deoxyhemoglobin, cytochrome

oxidase aa_3, reduced cytochrome oxidase aa_3, nitrosyl hemoglobin, nitrosyl tyrosine, glucose and lactate.